

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:

Shannon

Serial No. 09/690,173

Filed: October 16, 2000

For: Method for Linear mRNA  
Amplification

Art Unit:

Examiner: Janet Epps

Atty Docket No. 10990638-2

Assistant Commissioner for Patents  
Washington, DC 20231

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APPEAL  
Brief

**BRIEF ON APPEAL**

**REAL PARTY IN INTEREST**

The real party in interest in this appeal is "Agilent Technologies, Inc.", to which all rights have been assigned.

**RELATED APPEALS AND INTERFERENCES**

There are no related appeals or interferences.

**RELATED PATENTS AND APPLICATIONS**

The present application is a Continued Prosecution Application based on parent Application No. 09/322,692, now U.S. Patent No. 6,132,997.

**STATUS OF CLAIMS**

The present application was filed on October 16, 2000 with Claims 1-31. On October 16, 2000, a preliminary amendment was filed and Claims 1-31 were canceled and new Claims 32-40 were added. On January 28, 2002, during prosecution of the present application, Claim 38 was amended and new Claims 41-48 were added. On July 3, 2002, the addition of new Claims 49-51 was proposed but not entered. Accordingly, Claims 32-48 are pending in the present application and are appealed herein. The pending claims are recited in the attached Appendix.

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### STATUS OF AMENDMENTS

During prosecution of the present application, a preliminary amendment was filed canceling Claims 1-31 and adding Claims 32-40, which amendments were entered. On January 28, 2002, new Claims 41-48 were added and Claim 38 was amended, which amendments were entered. On July 3, 2002, the addition of new Claims 49-51 was proposed, but these amendments were not added. Thus, Claims 32-48 are pending and appealed, which claims are recited in the attached Appendix.

### SUMMARY OF THE INVENTION

The claims on appeal are directed to kits for practicing an improved method for linearly amplifying mRNA to produce antisense RNA. By using the subject kits, antisense RNA can be produced more quickly and easily than with prior art methods, because one need not perform a reverse transcriptase separation step.

The improved methods for linear mRNA amplification as provided by the subject kits, can provide a number of advantages over the prior art methods. Generally prior art methods of linear mRNA amplification are labor intensive and not readily amendable to robotic handling. Such prior art methods of linear mRNA amplification generally require phenol/chloroform extractions and buffer exchanges in order to separate the double-stranded cDNA from the reverse transcriptase.

The present invention can provide for an improvement over the prior art methods in that the methods, as provided in the subject kits, do not require the reverse transcriptase separation step. Instead, all of the necessary polymerization reactions, (i.e., first strand cDNA synthesis, second strand cDNA synthesis and antisense RNA transcription), may be carried out in the same reaction vessel. In other words, all of the steps for linearly amplifying mRNA into antisense RNA **can be carried out in a single reaction mixture without performing a separation step.** The requisite reagents, as provided in the claimed kits, need merely be added to the reaction mixture in the reaction vessel without any complicated separation steps being performed, such as phenol/chloroform extraction. As such, the methods, as described in the instructions of the subject kits, are **amenable to automation, making them particularly attractive for high throughput applications.** Furthermore, the methods of the claimed kits, despite their simplicity, may **yield high amplification extents,**

where the amplification extents (mass of RNA product/mass of RNA target) can typically be at least about 50-fold, and may be as high as 600-fold. In addition, such amplification extents can be achieved with **low variability** (e.g. coefficients of variation about the mean amplification extents that do not exceed about 10%, and usually do not exceed about 5%). Finally, all of the benefits of linear amplification can be achieved with the methods, such as the production of unbiased antisense RNA libraries from heterogeneous mRNA mixtures. As such, the method of producing linearly amplified amounts of antisense RNA, as described in the instructions of the subject kits, represent a significant contribution to the art, and may find use in a variety of different applications in which the preparation of linearly amplified amounts of antisense RNA is desired.

The improved methods of mRNA amplification, as provided in the claimed kits, include the following steps: First, mRNA is converted to double-stranded cDNA using a promotor-primer having a poly-dT primer site linked to a promoter sequence so that the resulting double-stranded cDNA is recognized by an RNA polymerase. Second, the resultant double-stranded cDNA is then transcribed into antisense RNA, **in the presence of a reverse transcriptase that is rendered incapable of catalyzing RNA-dependent DNA polymerase activity during this transcription step.** It is a feature of the invention that the reverse transcriptase that is present during this transcription step is rendered inactive. As a result of the inactivity of the reverse transcriptase, the antisense RNA products of the transcription reaction cannot serve as substrates for additional rounds of amplification, and the amplification process thus proceeds linearly, and not exponentially.

As such, the claims recite a kit for use in linearly amplifying mRNA, said kit comprising (1) an oligonucleotide promoter-primer comprising an RNA polymerase promoter sequence; and (2) instructions to convert the mRNA to cDNA, and to then transcribe the cDNA into RNA in the presence of a reverse transcriptase that is rendered incapable of RNA-dependent DNA polymerase activity during this transcription step.

**ISSUE ON APPEAL**

***I. WHETHER THE INSTRUCTIONAL ELEMENT OF THE PENDING CLAIMS CARRIES ANY PATENTABLE WEIGHT SUCH THAT THE CLAIMS ARE NOT ANTICIPATED BY WANG ET AL. AND PHILLIPS ET AL.***

In the Examiner's Advisory Action of July 26, 2002, it was stated that the Applicants' arguments filed July 9, 2002, were considered, but were not persuasive. The Advisory Action maintained the rejection of pending Claims 32-37 and 39-40 under 35 U.S.C. §102(b) as being anticipated by Phillips et al., and the rejection of pending Claims 38 and 41-48 under 35 U.S.C. §102(e) as being anticipated by Wang et al. In making the rejections, the Examiner maintained the reasons of record set forth in prior Official Actions in asserting that the printed matter (i.e. instructions for use), does not distinguish the instant invention from the prior art references of Wang et al. and Phillips et al. because the claim elements directed to printed matter do not carry any patentable weight.

Specifically, the Examiner asserted that the printed matter of the kit of the instant invention does not carry any patentable weight because it merely provides an intended use of the remaining contents of the claimed kit, and is not functionally related to the other kit elements. The Examiner reasoned that the printed matter is not functionally related to the other kit elements because the printed matter does not directly affect any material properties of the remaining contents of the kit, and is not processed by the remaining contents of the kit.

Further, the Examiner stated in the Advisory Action of July 26, 2002, that the Applicants did not explicitly state how the methods suggested by the references of either Wang or Phillip are distinct from the method recited in the kits of the claimed invention. Specifically, the Examiner stated that the reference of Wang et al. provides kits for use in a method for mRNA amplification, and that the reference of Phillips et al. discloses compositions for the intended use of linear amplification of mRNA comprising the contents of the kit recited in the instant claims.

## GROUPING OF CLAIMS

Claims 32-48 stand together.

## ARGUMENTS

***I. THE PENDING CLAIMS ARE NOT ANTICIPATED BY WANG ET AL. NOR PHILLIPS ET AL., BECAUSE THE CLAIMED ELEMENTS DIRECTED TO PRINTED MATTER CARRY PATENTABLE WEIGHT, AS A RESULT OF THE FUNCTIONAL RELATIONSHIP BETWEEN THE CLAIMED ELEMENTS DIRECTED TO PRINTED MATTER AND THE OTHER CLAIMED ELEMENTS.***

The Examiner has asserted that Claims 32-48 of the instant invention, absent the printed matter, are anticipated by the prior art Wang et al. and Phillips et al. The Examiner reasoned that the elements containing printed matter do not carry any patentable weight with respect to the anticipation analysis because they merely provide an intended use of, and are not functionally related to, the remaining contents of the kit. Specifically, the Examiner has asserted that the printed matter is not functionally related to the other kit elements because the presence of the printed matter in the kit does not materially affect the contents of the kit, and the printed matter is not processed by the contents of the kit.

### The Printed Matter Doctrine

The law provides guidance on the issue of the patentable weight of printed matter. Printed matter by itself does not constitute a "manufacture" and is not within the statutory classes of patentable subject matter. [M.P.E.P. §706.03(a)]. However, as an exception to this rule, printed matter may constitute an element of a patentable claim if the claim element involves a new and useful feature of a physical structure or if the claim involves a **new and useful relation** between the printed matter and a physical structure. [*Chisum on Patents*, §1.02(4), p.1-20.]

"[It is] well settled that patentable weight can be given printed matter only when a novel relationship exists between said printed matter and the claimed structure."

[*In re Miller*, 418 F.2d 1392, (C.C.P.A. 1969).]

Burden of proof

The Examiner has denied that there is a functional relationship between the instructions for use and the reagents, and has merely asserted that the presence of the instructions in the kit do not materially affect the contents of the kit and are therefore not deemed to hold any patentable weight for prior art purposes. It is respectfully submitted that the Examiner must do more than that.

As the Federal Circuit in *In re Lowry*, stated:

"...the burden of establishing the absence of a novel, nonobvious functional relationship rests with the PTO. 'If examination at the initial stage does not produce a prima facie case of unpatentability, then without more the applicant is entitled to grant of the patent.'"

[*In re Lowry*, 32 F.3d 1579, 1584 (Fed.Cir. 1994).]

Thus, the Examiner cannot merely deny that there is a functional relationship between the printed matter elements and the other elements of the invention, but must prove that there is no such novel and nonobvious functional relationship.

Printed Matter constitutes a limitation upon which patentability may be predicated

The Examiner rejected the Applicants' argument that the printed matter of the instant invention constitutes a limitation upon which patentability may be predicated. The Applicants cited the case of *In re Lowry*, 32 F.3d 1579, (Fed.Cir. 1994), which the Examiner asserted is inapplicable to the instant case. Specifically, the Examiner asserted that *In re Lowry* is not applicable to the instant invention because the printed matter of the Lowry invention was processed not by the mind, but by a machine or computer. Specifically, the Examiner stated: "The printed matter is not processed by the contents of the kit as in the case of *In re Lowry*, therefore the decision set forth regarding the invention in *In re Lowry* can not be applied in the instant case since the facts of *In re Lowry* are not coextensive with those facts regarding the instantly claimed invention."

With respect, it is submitted that the Examiner erred in her interpretation of *In re Lowry*, and that contrary to the Examiner's assertions, the case of *In re Lowry* is applicable to the instant case and supports the finding that the printed matter of the instant invention constitutes a limitation upon which patentability may be predicated. The court in *In re Lowry* aptly discussed the printed matter doctrine as is applicable to the instant case. The court, in reversing the Examiner's rejection, discussed a number of reasons why the Examiner was wrong, one of which was that the data structures in *In re Lowry* were not analogous to printed matter, and thus the printed matter doctrine did not apply. Contrary to the Examiner's assertions in the instant case, the data structures in the *In re Lowry* case were construed to *not* be printed matter, and thus the printed matter doctrine did not apply to that invention. Thus there was no requirement of a functional relationship between the data structures and the other elements in *In re Lowry* because the printed matter doctrine did not apply. However, even though the data structures of the invention in *In re Lowry* were construed to not be printed matter, the court still went on to discuss the relevant issues of the printed matter doctrine that are applicable to the instant case. The court went on to state: "Even assuming, *arguendo*, that data objects and data structures are analogous to printed matter, the Board erred in its reliance on *Gulack*..." [emphasis added]. Thus, although the printed matter doctrine did not apply specifically to the invention of *In re Lowry*, the court still went on to make some relevant statements of law in that regard that were properly relied upon by the Applicants of the instant case.

Thus the court's statement in *In re Lowry* still applies:

"The [PTO] must consider all claim limitations when determining patentability of an invention over the prior art. The PTO may not disregard claim limitations comprised of printed matter."

[*In re Lowry*, 32 F.3d 1579, 1582 (Fed.Cir. 1994).]

The Examiner cannot ignore the printed matter element of the instructions for use in the instant invention and then reject the application based on anticipation of the claims without the printed matter. Specifically, the Examiner must consider claim limitations comprised of printed matter when the claim is directed to a combination of elements. As the court in *In re Miller* stated:

“The fact that printed matter by itself is not patentable subject matter, because non-statutory, is no reason for ignoring it when the claim is directed to a combination.”

[*In re Miller*, 418 F.2d 1392, 1396 (C.C.P.A. 1969).]

Further the court in *In re Gulack* also stated:

“Differences between an invention and the prior art cited against it cannot be ignored merely because those differences reside in the content of the printed matter. [The Examiner] cannot dissect a claim, excise the printed matter from it, and declare the remaining portion of the mutilated claim to be unpatentable. **The claim must be read as a whole.**” [emphasis added]

“...the CCPA notably weary of reiterating this point, clearly stated that printed matter may well constitute structural limitations upon which patentability can be predicated.”

[*In re Gulack* 703 F.2d, 1381, 1385 (Fed. Cir. 1983).]

The Applicants do not seek to patent the content of information inside the instructions themselves alone, but rather, the combination of elements in the kit as a whole, leading to the new and useful application of reagents imposed by the instructions. Thus, the Examiner must regard the printed matter elements of the instant claims as a limitation upon which patentability may be predicated.

The location of the printed matter is immaterial

The Examiner has suggested that because of the location of the printed matter of the claimed invention, the printed matter failed to impart functionality. The Examiner has attempted to distinguish the cases of *In re Gulack* and *In re Miller* because “the printed matter was directly printed upon the claimed invention...” With respect, we submit that the Examiner erred in her interpretation of the noted cases on this point. The printed matter does not have to be directly printed on the remaining claimed structural elements to confer functionality to the claimed invention. The printed matter of the subject invention directly affects the material properties of the remaining structural elements of the kit, regardless of the location of the printed matter (even though not directly printed on the remaining structural elements). The Court in *In re Miller* specifically noted that the specific location of the printed matter



was immaterial to their functionality. It is the functional relationship between the printed matter and the other elements, and not their structural relationship that is significant.

The invention in *In re Miller* involved an element of a measuring receptacle and another element of a legend. The court noted that the element of the legend was either “on the receptacle *or* attached to it...” [emphasis added], [*In re Miller*, at 1394.] Thus the printed matter (legend) of the invention in *In re Miller* was not necessarily “directly printed upon the claimed invention”, as the Examiner in the instant case has asserted.

Further, the court in *In re Miller* stated:

“While the examiner was quite willing to consider such elements as proper parts of the ‘structure’ and in ‘a definite structural relationship with the wall of the measuring vessel’ when, as in the allowed claims, they were required to be in ‘a specific location,’ he would give them no weight at all, apparently, when the location was not specified or necessarily restricted... We do not see why this is so and the examiner does not tell us. We do not see the ‘structural’ relationship – whatever that means – is required to obtain the practical, problem-solving results of the appellant’s invention... It seems to us that **what is significant here is not structural but *functional* relationship...**” [emphasis added]; [*In re Miller*, at 1395-6.]

Thus the cases of *In re Gulack* and *In re Miller* are not distinguished on the basis of the location of the printed matter, and the location of the printed matter of the subject invention is immaterial to its functionality. The instructions of the subject invention impart a new and useful functionality to the reagents apart from its structural relationship to the reagents or its specific location within the kit.

#### Functional Relationship

As per the printed matter doctrine, the critical question is whether there exists any new and useful functional relationship between the printed matter and the other structural elements of the claims (reagents). As the court in *In Re Levin* stated:

“The only requirement that 35 U.S.C. §101 imposes as set forth in *In re Miller* is that a new and unobvious functional relationship must exist between the claimed combination of printed matter and other claimed elements.”

[*In re Levin*, 1997 U.S. App. Lexis 1781, (Fed. Cir. 1997).]

The Examiner in the instant case has rejected the Applicant’s arguments that there is such a functional relationship. Specifically, the Examiner based her rejection on the reasoning that “[t]he printed material of the kit of the instant invention, do not directly affect any material properties of the remaining contents of the kit.” However, with respect, we submit that the Examiner erred in her analysis, and submit that the printed material elements of the instant invention do in fact directly affect the remaining elements of the kit, and are thus functionally related.

As noted in the above discussion with respect to the case of *In re Lowry* and the printed matter doctrine, it makes no difference that the printed matter is processed by a mind. As long as there is a functional relationship between the printed matter and the remaining elements of the claim, the printed matter will be accorded patentable weight. Thus it is submitted that the instructions for use of the instant invention, although not processed by the reagents of the kit, (like software is processed by a computer), nevertheless, carries patentable weight.

The court in *In re Lowry*, (assuming arguendo that data objects and data structures were analogous to printed matter) found that the data objects (as printed matter) were functionally related to the computer memory (claimed structural element). The court reasoned that the data objects (printed matter), although existing only as:

“a collection of bits having information about relationships between the ADOs,...facilitated addition, deletion, and modification of information stored in the memory. In sum, the ADO’s **perform a function**. Gulack requires no more. See *Gulack*, 703 F.2d at 1386.”

[*In re Lowry* at 32 F.3d 1579, 1583-4 (Fed. Cir. 1994).]

Thus the court found a functional relationship based on the finding that the printed matter performed a function within the invention.

The court in *In re Miller* found a functional relationship between the printed matter and other elements of the claims, although the printed matter was not processed by, nor directly located on the remaining structural elements. There the invention involved a structural element directed to a measuring receptacle, and a printed matter element directed to a legend specifying the ratio or proportion of a full recipe to be measured in the said measuring receptacle. In concluding a functional relationship between the legend and the receptacle, the court stated:

“Here there is a new and unobvious functional relationship between a measuring receptacle, volumetric indicia thereon indicating volume in a certain ratio to actual volume, and a legend indicating the ratio, and in our judgment the appealed claims properly define this relationship.”

[*In re Miller*, 418 F.2d 1392, 1396 (C.C.P.A. 1969).]

The printed matter element of *In re Miller*, performed a function of directing how to use the other elements of the claim in a way that was different from the prior art. As a result, the court found that there was a functional relationship between the printed matter element and the remaining structural element.

Further, the case of *In re Levin* is also instructive. The invention in that case involved a coding system for visually displaying a color code uniquely signifying the expiration date of each of a plurality of pharmaceutical products. The color coded indicia (printed matter element) provided information about the pharmaceutical product (structural element). The court in observing that the color coded expiration date indicia provides information about the pharmaceutical product or what is contained in it, found that “the relationship between the expiration date indicia on the container or pharmaceutical product is a functional relationship.” [*In re Levin*, 1997 U.S. App. Lexis 1781.]

The claims of the instant invention are directed to, *inter alia*, a kit containing (i) biochemical reagents; and (ii) instructions for use of the reagents in a specific

method. The instant invention involves the application of the reagents, as directed by the instructions for use, in a method that the prior art neither discloses nor suggests. The reagents are uniquely treated, arranged and combined as per the instructions for use. The instructions for use exist as a collection of information that perform a function by facilitating the specific treatment, arrangement and combination of the reagents of the kit in a new and useful way. (as did the data objects of the invention in *In re Lowry*, by facilitating the addition, deletion, and modification of information stored in memory.) The instructions for use impart a tangible functional consequence in the improved method of linearly amplifying antisense RNA by providing information on how to use the reagents of the kit in a new and useful manner (as did the color coded indicia of the invention in *In re Levin*, by providing information about the expiry date of the pharmaceutical product). Accordingly, the elements directed to the instructions for use are dynamic and functionally significant elements of the instant kit claims, and not just mere passive or descriptive recordings of information or mere compilations of facts. The instructions for use perform a determining function of directing a new and useful method of applying the reagent elements. (as did the legend of the invention in *In re Miller*, in specifying the ratio or proportion of a full recipe to be measured in the measuring receptacle.) As per the court's reasoning in *In re Lowry* noted above, the law requires no more than the performance of a function.

Furthermore, there is a definite and decided relationship between the reagents and the instructions for use. The manner of application of the reagents depends on the instructions for use. There is a cooperative relationship between the instructions for use and the reagents of the kit, without which it would be impossible to carry out the improved method of antisense RNA amplification. It is submitted that without the instructions, one skilled in the art would not know how to use the reagents of the kit in the improved method of antisense RNA amplification. As such, the instructions for use do not merely provide an intended use of the reagents, but are functionally related to the reagents of the kit because they specifically direct how to apply them. The instructions are an integral and necessary element of the kit in that the reagents can only be used effectively with them. By virtue of this unique functional relationship between the instructions and the reagents, great savings of time and money are effected by the use of this improved method of antisense RNA amplification (i.e. fewer steps are required in antisense RNA amplification, resulting in less required

labor; and the method is amendable to robotic handling). Thus the combination of the instructions and reagent elements of the subject invention and the functional relationship that exists between them, is a new and useful inventive concept that must be accorded patentable weight.

Claims 32-48 considered in their entirety (including the printed matter elements with patentable weight), are not anticipated by the references of Wang et al. and Phillips et al.

The Examiner has asserted that the instant claims, even assuming that they carried the patentable weight of the printed matter, are anticipated by the Wang et al. and Phillips et al. references. Specifically, the Examiner stated: "[a]ssuming, *arguendo*, that the instructions of the present invention functionally modified the claimed invention, one of skill in the art would recognize that the disclosures of the Wang et al. and Phillips et al. references can be used as a set of instructions to use the contents of the kit of the present invention in a method of mRNA amplification."

Further, the Examiner has asserted that the Applicants "have not explicitly stated how the method suggested by either Wang or Phillips is distinct from the intended use of the kit of the claimed invention."

It is respectfully submitted that the Examiner has erred in her analysis. The teachings of Wang et al. and Phillips et al. are concerned with completely different methods, as evidenced by the issuance of the methods of the present kits in the parent application, which parent application issued as a patent over both Wang and Phillips. Specifically, the methods disclosed in Wang and Phillips require a phenol/chloroform extraction step to remove the reverse transcriptase prior to second strand cDNA synthesis. Accordingly, transcription of cDNA into RNA in the Wang and Phillips methods does not occur in the presence of a reverse transcriptase, since the reverse transcriptase has been removed by the prior phenol/chloroform extraction step. As such, the methods disclosed by Wang and Phillips are completely different from the methods appearing in the instructional element of the claimed kits, since the subject methods are ones where RNA is transcribed from cDNA in the presence of a reverse transcriptase. The fact that the methods of the instructions of the present kits per se were found patentable over the both Wang and Phillips in the parent application evidences that the methods of Wang and Phillips neither anticipate nor obviate the

'methods disclosed in the instructions of the present kits. Thus neither Wang's nor Philips' disclosures could be "used as a set of instructions to use the contents of the kit of the present invention in a method of mRNA amplification", as specified in the instructions of the present kits.

It is well established that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." [*Verdegaal Bros. V. Union Oil of California*, 2 USPQ 2d 1051 (Fed. Cir. 1987), *cert denied*, 481 U.S. 1052 (1987); *See also Scripps Clinic and Research Foundation v. Genentech Inc.*, 18 USPQ 2d 1001, (Fed. Cir. 1991).] As such, any art cited must describe a kit containing reagents and an instructional element to use the reagents in the recited method, (as was patented in the parent application).

In the instant case, Wang fails to teach a kit containing the instructional element of the present claims because Wang is concerned with an entirely different method, i.e., one that includes a phenol/chloroform extraction step, as discussed above. As such, Wang fails to teach each and every element of the claims. Because Wang fails to teach each and every element of the claimed kit, e.g., the instructions, Wang fails to anticipate Claims 38 and 41-48 under 35 U.S.C. § 102(e).

Further, Claims 32-36 and 39-40 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Phillips. Again, this reference fails to teach a kit containing the instructional element of the present claims because Phillips is concerned with an entirely different method, i.e., one that includes a phenol/chloroform extraction step, as described above. As such, Phillips fails to teach each and every element of the claims. Because Phillips fails to teach each and every element of the claimed kit, e.g., the instructions, Phillips fails to anticipate Claims 32-36 and 39-40 under 35 U.S.C. § 102(b).

Having established that the printed matter element carries patentable weight, the instant kit claims considered in their entirety, are thus not anticipated by the references of Wang et al. and Phillips et al.

**SUMMARY**

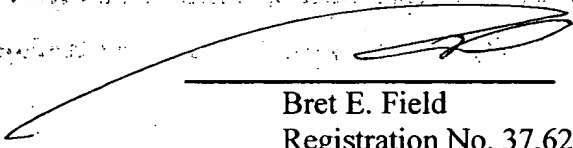
The instructional elements of each of the instant claims carry patentable weight because there is a functional relationship between the instructional elements and the reagent elements. The instant claims are not anticipated by Wang et al. and Phillips et al. because the said references each fail to teach the elements of the instant claims that are directed to the instructions for using the reagents in a novel method of linear mRNA amplification. As such, none of the pending claims are anticipated by Wang et al. or Phillips et al. and are patentable over these cited references.

**RELIEF REQUESTED**

Appellants respectfully request that the rejection of Claims 32-48 under 35 U.S.C. §102(b) and 35 U.S.C. §102(e) be reversed and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,

Date: 10.7.02

  
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## APPENDIX

32. A kit for use in linearly amplifying mRNA, said kit comprising:  
an oligonucleotide promoter-primer comprising an RNA polymerase promoter sequence; and  
instructions to convert the mRNA to cDNA, and to then transcribe the cDNA into RNA in the presence of a reverse transcriptase that is rendered incapable of RNA-dependent DNA polymerase activity during this transcription step.
33. A kit according to claim 32 wherein the instructions include an instruction for inactivating the reverse transcriptase by heating.
34. A kit according to claim 33 wherein the instruction for heating comprises an instruction to raise the temperature to between 55°C to 70°C for 5 to 60 minutes.
35. A kit according to claim 34 wherein the instruction to raise the temperature comprises an instruction to raise the temperature to 65°C.
36. The kit according to Claim 32, wherein said kit further comprises at least one polymerase.
37. The kit according to Claim 36, wherein said polymerase is MMLV-RT.
38. The kit according to Claim 32, wherein the kit comprises an RNaseH<sup>-</sup> polymerase and an RNaseH<sup>+</sup>-polymerase.
39. The kit according to Claim 36, wherein said kit further comprises an RNA polymerase.
40. The kit according to Claim 39, wherein said RNA polymerase is T7 RNA polymerase.



41. A kit for use in linearly amplifying mRNA, said kit comprising:
  - (a) an oligonucleotide promoter-primer comprising an RNA polymerase promoter sequence;
  - (b) an RNaseH- polymerase; and
  - (c) an RNaseH+ polymerase.
42. The kit according to Claim 41, wherein said kit further comprises:  
instructions to convert the mRNA to cDNA, and to then transcribe the cDNA into RNA in the presence of a reverse transcriptase that is rendered incapable of RNA-dependent DNA polymerase activity during this transcription step.
43. The kit according to Claim 42, wherein the instructions include an instruction for inactivating the reverse transcriptase by heating.
44. The kit according to claim 43, wherein the instruction for heating comprises an instruction to raise the temperature to between 55°C to 70°C for 5 to 60 minutes.
45. The kit according to Claim 44, wherein the instruction to raise the temperature comprises an instruction to raise the temperature to 65 °C.
46. The kit according to Claim 41, wherein said kit further comprises MMLV-RT.
47. The kit according to Claim 46, wherein said kit further comprises an RNA polymerase.
48. The kit according to Claim 47, wherein said RNA polymerase is T7 RNA polymerase.